Complete Summary

GUIDELINE TITLE

Teratogenicity associated with pre-existing and gestational diabetes.

BIBLIOGRAPHIC SOURCE(S)

Allen VM, Armson BA, Wilson RD, Allen VM, Blight C, Gagnon A, Johnson JA, Langlois S, Summers A, Wyatt P, Farine D, Armson BA, Crane J, Delisle MF, Keenan-Lindsay L, Morin V, Schneider CE, Van Aerde J, Society of Obstetricians and Gynecologists of Canada. Teratogenicity associated with pre-existing and gestational diabetes. J Obstet Gynaecol Can 2007 Nov;29(11):927-34. [62 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Congenital abnormalities associated with pre-existing and gestational diabetes mellitus (GDM)

GUIDELINE CATEGORY

Counseling
Prevention
Risk Assessment
Screening

CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To review the teratogenesis associated with pre-existing gestational diabetes
- To provide guidelines to optimize prevention and diagnosis of fetal abnormalities in women with diabetes
- To identify areas specific to fetal abnormalities and diabetes requiring further research

TARGET POPULATION

Women with pre-existing and gestational diabetes who become or are attempting to become pregnant

INTERVENTIONS AND PRACTICES CONSIDERED

1. Pre-conception recognition of women at high risk
2. Offer biochemical and ultrasonic screening, detailed evaluation of fetal cardiac structures
3. Obtain family history
4. Pre-conception counseling by multidisciplinary team that reviews risks and encourages planned pregnancy
5. Maintain euglycemia before and during pregnancy
6. Pre-conception and first trimester folic acid supplementation

MAJOR OUTCOMES CONSIDERED

- Structural congenital abnormalities
- Chromosomal abnormalities
- Perinatal and infant mortality and morbidity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Cochrane Library and Medline were searched for English-language articles, published from 1990 to February 2005, relating to pre-existing and gestational diabetes and fetal abnormalities. Search terms included pregnancy, diabetes mellitus, pre-existing diabetes, pregestational diabetes, type 1 diabetes, type 2 diabetes, insulin dependent diabetes, gestational diabetes, impaired glucose tolerance, congenital anomalies, malformations, and stillbirth. Additional publications were identified from the bibliographies of these articles as well as the Science Citation Index. All study types were reviewed. Randomized controlled trials were considered evidence of the highest quality, followed by cohort studies. Key studies and supporting data for each recommendation are summarized with evaluative comments and referenced.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort (prospective or retrospective) or case–control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

* Adapted from the Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Classification of Recommendations*

A. There is good evidence to recommend the clinical preventive action

B. There is fair evidence to recommend the clinical preventive action

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making

D. There is fair evidence to recommend against the clinical preventive action

E. There is good evidence to recommend against the clinical preventive action

I. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*Adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This guideline has been reviewed by the Genetics Committee and the Maternal Fetal Medicine Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada (SOGC).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The quality of evidence (**I-III**) and classification of recommendations (**A-E, I**) are defined at the end of the "Major Recommendations."

Pathophysiology

1. Experimental studies suggest that hyperglycemia is the major teratogen in diabetic pregnancies, but other diabetes-related factors may also affect fetal outcomes. Further research using animal models is required to clarify the teratogenic factors associated with pre-existing and gestational diabetes. **(II-3C)**

Pre-Existing Diabetes

2. Prospective and retrospective cohort studies have demonstrated an increased risk of congenital abnormalities with pre-existing diabetes (see Table 2 in the original guideline document for specific malformations). Further studies that include outcomes from first and second trimester pregnancy terminations, account for potential confounding variables, and use appropriate control groups are required. **(II-2A)**

Gestational Diabetes

3. Prospective and retrospective cohort studies have demonstrated an increased risk of congenital abnormalities with gestational diabetes. This observation is probably related to the inclusion of women with unrecognized type 2 diabetes. Clarification of the relationship between gestational diabetes and congenital abnormalities by studies that include outcomes from first and second trimester pregnancy terminations, account for potential confounding variables, and use appropriate control groups are required. **(II-2A)**
4. In some women, type 2 diabetes may be identified for the first time in pregnancy. Pre-conception recognition of women at high risk for type 2 diabetes and optimal glycemic control may reduce the risk of congenital anomalies. **(II-2A)**

Medications

5. Second generation sulfonylureas have not been associated with congenital abnormalities in human studies. The use of biguanides may be associated with other adverse perinatal outcomes. The use of other oral antihyperglycemic agents is not recommended in pregnancy. **(II-2A)**

Effect of Obesity

6. The risk of congenital abnormalities is increased in the offspring of obese women with diabetes. A healthy diet and regular exercise may help optimize pre-pregnancy weight and reduce the risk of congenital anomalies. **(II-2A)**

Prenatal Diagnosis

7. Accurate determination of gestational age is required in women with diabetes. Given the increased risk of congenital abnormalities, they should be offered appropriate biochemical and ultrasonographic screening and a detailed evaluation of fetal cardiac structures. **(II-2A)**

Pre-Conception Counseling

8. Women with diabetes should be offered pre-conception counselling with a multidisciplinary team to optimize general health and glycemic control and to review the risks of congenital anomalies. **(II-2A)**
9. A careful history should be obtained to identify other factors, such as a positive family history or advanced maternal age, that may further increase the risk of congenital structural or chromosomal abnormalities. **(II-2A)**
10. Pregnancy in women with diabetes should be planned. Good contraceptive advice and pre-pregnancy counselling are essential. Euglycemia should be maintained before and during pregnancy. **(II-2A)**
11. All women with diabetes should be counselled regarding intake of foods high in folic acid, folate-fortified foods, and appropriate folic acid supplementation of 4 to 5 mg per day pre-conceptionally and in the first 12 weeks of gestation. **(II-2A)**
12. A substantial number of women with diabetes do not access pre-conception care programs. Strategies are needed to improve access to such programs and to maximize interventions associated with improved pregnancy outcomes, such as folic acid use. **(II-2A)**

Definitions

Quality of Evidence Assessment*

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Classification of Recommendations **

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E. There is good evidence to recommend against the clinical preventive action

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*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

**Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate counseling and prevention of fetal abnormalities in women with pre-existing or gestational diabetes
- Increased awareness of fetal abnormalities associated with pre-existing and gestational diabetes

POTENTIAL HARMS

- First generation sulfonylureas (such as chlorpropamide) have been shown to cross the placenta; however, the newer second generation sulfonylureas (such as glyburide) may not cross the placenta, and less fetal exposure may occur.
- Biguanides cross the placenta, and although they do not appear teratogenic, they have been associated with other adverse perinatal outcomes such as

gestational hypertension and increased perinatal mortality when used for treatment in diabetic pregnancies.

QUALIFYING STATEMENTS

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This document reflects emerging clinical and scientific advances on the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the Society of Obstetricians and Gynaecologists of Canada (SOGC).

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Nov

GUIDELINE DEVELOPER(S)

Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

SOURCE(S) OF FUNDING

Society of Obstetricians and Gynaecologists of Canada

GUIDELINE COMMITTEE

Society of Obstetricians and Gynaecologists of Canada Genetics Committee
Society of Obstetricians and Gynaecologists of Canada Maternal Fetal Medicine Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Society of Obstetricians and Gynaecologists of Canada Web site.

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada (SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on March 9, 2009. The information was verified by the guideline developer on March 25, 2009.

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